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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/022,249	12/17/2001	Manuel Vega	37851-911	7196
20985	7590	12/23/2005	EXAMINER	
FISH & RICHARDSON, PC P.O. BOX 1022 MINNEAPOLIS, MN 55440-1022			LIN, JERRY	
			ART UNIT	PAPER NUMBER
			1631	
DATE MAILED: 12/23/2005				

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>		<b>Applicant(s)</b>	
	10/022,249		VEGA ET AL.	
	<b>Examiner</b>		<b>Art Unit</b>	
	Jerry Lin		1631	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 01 September 2005.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-33 and 42-44 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-33 and 42-44 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)             | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)    | Paper No(s)/Mail Date. _____  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                                    |

## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on July 13, 2005 has been entered.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-33 and 42-44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Instant claims 1, 22, 23, 24, 27, 30, and 32 have a last step of selecting a predetermined property from the chemical, physical, and biological property. It is unclear if only single property is to be selected from any one of the types of properties, if a property is to be selected from each type of property, or if a single property is intended to represent chemical, physical, and biological properties. Clarification of the metes and bounds of the instant claims, via clearer claim language is requested.

Claim 28 recites the limitation "at step f" in line 1. There is insufficient antecedent basis for this limitation in the claim. There is no step f, d, or e in the instant claim or in the claim from which it depends.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-21, 27, and 42-44 are rejected under 35 U.S.C. 102(e) as being anticipated by Short (US 6,171,820 B1).

As was stated in previous actions, Short discloses a method of producing a set of mutagenized progeny polynucleotides encoding a polypeptide from a parental template polynucleotide (i.e. target protein), via ("codon site-saturation mutagenesis" wherein at each original codon position there is produced at least one substitute codon encoding each of the 20 naturally encoded amino acids (instant claims 1, 2, 4, 9-12, and 19-21; Abstract; Column 1, lines 32-42; Column 5, lines 12-33; and Columns 33-35, beginning on line 51). Figure 2 illustrates the use of the site-saturation mutagenesis approach for achieving all possible amino acid changes at each amino acid site along the polypeptide (codon mutagenesis (N,N,G/T); instant claims 13-15 and 42-44; Column 6, lines 47-

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60). Example 5 describes the screening of the progeny where the mutagenized polynucleotides encoding polypeptides were introduced (i.e. plasmid, viral vector, etc) into host cell (i.e. bacterial) on an addressable array (i.e. well plate, loci, etc) and analyzed for kinetic activities (improved stability/ "predetermined property") (instant claims 3, 5-8, 16-18, and 27; Column 11, lines 38-46; Column 20, lines 51-58., and Columns 55-56, beginning on line 34). The inventor also provides the optional repeating of the described steps (Column 5, lines 8-11). Additionally, the inventors indicate the identification of protein mutational positions (i.e. hit position) (Column 4, line 64 to Column 5, line 34; and Column 12, lines 20-24).

Applicants have responded to his rejection by amending instant claims 1 and 27 to include the limitation of "individually" in step (b). However, giving the instant claims the broadest reasonable interpretation, the amendment only requires that each set of nucleic acid molecules be introduced individually into host cells. In other words, the limitation prohibits the simultaneous introduction of two or more sets of nucleic acid molecules into host cells. Short teaches introducing each set of nucleic acid molecules individually into host cells (Columns 55-56, beginning on line 34). Thus Short anticipates the amendment to the claims.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

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invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 22 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Short (US 6,171,820 B1) in view of Collett et al. (US 2002/0081574 B1).

Short is applied as above.

Short does not explicitly teach wherein the change in activity of the target proteins is at least 10-1000% compared to an unmodified target protein.

Collett et al. teaches screening modified proteins with a 10-25 fold change in activity (page 6, paragraph 49, Table 1; Figure 3).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the methods of Collett et al. with Short to gain the benefit of determining the activity of protein for finding useful proteins. Short states that the purpose of his invention is to find useful proteins (column 1, lines 30-50). Also it is noted that determining the enzymatic activity is well known in the art at the time of the invention. In order to determine if a protein was useful or not, one of ordinary skill in the

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art would be motivated to also determine the activity of the protein. Thus one of ordinary skill in the art would have been motivated to combine the references of Collett et al. with Short.

Claims 24, and 27-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Short (US 6,171,820 B1) in view of Berlioz et al. (US 5,925,565).

Short is applied as above.

Short does not explicitly teach assessing the titer of the viral vectors in each set of cells.

Berlioz et al. teaches assessing the titer of the viral vectors after transfection for each set of cells (column 14, lines 39-65).

Short et al. teaches targeting proteins involved in viral replications (column 19, lines 30-48).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the methods of Berlioz et al. with Short in order to gain the advantage of determining the stability and efficiency of the vectors. Berlioz et al. state that one of his goals is to create the efficient and stable expression of genes (column 1, lines 10-17). Given that one of Short's goals is to produce useful proteins, one of ordinary skill in the art, would be motivated to test the efficiency and stability of the vectors in order to ensure that the host cells were properly expressing the gene of interest.



Claims 32 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Short (US 6,171,820 B1).

According to the MPEP Section 2106, Part VI, "merely using a computer to automate a known process does not by itself impart nonobviousness to the invention. See *Dann v. Johnston*, 425 U.S. 219, 227-30, 189 USPQ 257, 261 (1976); *In re Venner*, 262 F.2d 91, 95, 120 USPQ 193, 194 (CCPA 1958)." Claims 32 and 33 are merely computer automations of claim 1. Thus, it would be obvious to one skilled in the art to use a computer to automate the known processes disclosed by Short.

#### ***Contact Information***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jerry Lin whose telephone number is (571) 272-2561. The examiner can normally be reached on 10:00am-6:30pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, Ph.D. can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.



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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). Representatives are available to answer your questions daily from 6 am to midnight (EST). When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

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MICHAEL BORIN, PH.D  
PRIMARY EXAMINER



JL